# REMARKS

## Claim Amendments

Upon entry of this amendment, Claims 9 and 12-17 are pending in this application. Claim 9 is currently amended herein. Claims 1-8 and 10-11 are cancelled herein without prejudice or disclaimer as to the subject matter disclosed therein. New claims 12-17 are added.

Support for the amended and new claims is found throughout the application as originally filed. *See e.g.*, pages 7-8, Examples 1-6 and the original claims as filed. In particular, support for the addition of "human" may be found, for example, on page 6, line 23 to page 7, line 3 (e.g., referencing BIOGAMMA®). BIOGAMMA® is a human interferon-γ. *See e.g.*, BIOGAMMA® product manual at page 3 and partial translation of page 3 (showing interferon gamma-1a is an active ingredient in BIOGAMMA®); *see also* Merck Index at page 5014 (showing interferon gamma-1a is a human interferon-γ). The BIOGAMMA® product manual and relevant excerpt from the Merck Index are attached herewith as **Exhibit A and B**, respectively.

Applicant respectfully submits the above amendments do not constitute new matter.

## Drawings

The Office Action objects to the drawings.

Applicant has attached substitute drawings separately labeling Figures 1-5. Applicant respectfully requests this objection be withdrawn.

## Claim Objections

The Office Action objects to claims 1-8.

Applicant has cancelled claims 1-8, thereby rendering the claim objections moot.

**Rejections Under 35 U.S.C. § 112, First Paragraph**

Claims 1-11 stand rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for an agent for treatment of bullous pemphigoid comprising the interferon (IFN)-γ used in the clinical case examples, does not reasonably provide enablement for treatment of any other type of pemphigoid, and comprising all other types IFN)-γ.

Applicant has cancelled claims 1-8. Applicant has also amended claim 9 to recite "human interferon-γ" and "bullous pemphigoid." New independent claim 14 also includes the recitation of "human interferon-γ" and "bullous pemphigoid."

In light of these amendments, Applicant respectfully requests withdrawal of this rejection.

Claim 8 has been rejected under 35 U.S.C. §112, first paragraph, as allegedly being non-enabling and failing to comply with the written description requirement.

Applicant has cancelled claim 8, rendering these rejections moot.

**Rejection Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-8 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

Applicant has cancelled claims 1-8, rendering these rejections moot. Applicants note, however, that the acronym JRU stands for "Japanese Reference Unit," a term commonly used for interferon-γ in Japan. Furthermore, 1 JRU corresponds to 1.5 IU (International Unit). *See e.g.*, JSICR News Letter, No. 1, March 18, 1996, Japanese Society of Interferon and Cytokine Research (JSICR) at page 7, left column, lines 17-36 and in particular, lines 30-31. The JSICR News Letter is attached herewith as **Exhibit C**.

**Rejection Under 35 U.S.C. § 102**

Claims 1-11 stand rejected under 35 U.S.C. §102(b), as being anticipated by U.S. Pat. No. 5,145,677 ("'677 patent").

The Office Action states that the '677 patent teaches the administration of interferon-γ compositions for the treatment of malignant, infectious, and autoimmune

diseases in a dosage of 0.1-2,000,000 IU. *See* O.A. at page 7. The Office Action further states that although the '677 patent does not teach the treatment of pemphigoid, claim 9 is drawn to a composition comprising interferon-γ and as such, the compositions of the '677 patent would be effective in treating various forms of pemphigoid. *See* O.A. at pages 7-8. The Office Action concludes by stating that although the methods of the instant invention and those disclosed in the '677 patent are not identical, they are not patentably distinct because the process steps of administering compositions comprising interferon-γ are the same regardless of whether the purpose is to treat the diseases disclosed by the '677 patent or treat pemphigoid as claimed in the instant application. *See* O.A. at page 8.

Applicant respectfully disagrees and traverses this rejection.

Applicant has cancelled claims 1-8 and 10-11. Applicant has also amended 9 to recite a therapeutic composition comprising human interferon-γ as an active ingredient and a pharmaceutically acceptable carrier, said human interferon-γ being present in an amount effective to treat bullous pemphigoid, wherein said amount effective to treat bullous pemphigoid is 2,000,000-4,000,000 JRU.

Applicant respectfully submits that the '677 patent does not teach the claimed composition or methods of use. The '677 patent describes that low doses of interferon-γ (0.1-2,000,000 IU) may be used for the treatment of disease. *See e.g.*, col. 3, lines 3-16 ("According to this invention, *low doses* of natural or recombinant gamma inferons are used in processes and compositions...) (emphasis added). However, the '677 patent does not does not teach or suggest a dosage of 2,000,000-4,000,000 JRU (corresponding to 3,000,000-6,000,000 IU) for the treatment of pemphigoid, let alone bullous pemphigoid. Indeed, as the Office Action admits, the '677 patent does not teach compositions for treatment of pemphigoid, let alone bullous pemphigoid. Accordingly, Applicant respectfully requests withdrawal of the 102(b) rejection over the '677 patent.

Claims 1, 5-7 and 9-10 stand rejected under 35 U.S.C. §102(e), as being anticipated by U.S. Pat. Pub. No. 20030053985 ("'985 publication").

The Office Action states that the '985 publication teaches the administration of interferon-γ compositions in a dosage of 0.1-8,000,000 IU for treatment of a variety of diseases. *See* O.A. at page 8.[1]

Applicant respectfully disagrees and traverses this rejection.

Applicant has cancelled claims 1-8 and 10-11. Applicant has also amended 9 to recite a therapeutic composition comprising human interferon-γ as an active ingredient and a pharmaceutically acceptable carrier, said human interferon-γ being present in an amount effective to treat bullous pemphigoid, wherein said amount effective to treat bullous pemphigoid is 2,000,000-4,000,000 JRU.

Applicant submits the above amendments render this rejection moot. To the extent the Office Action maintains the '985 publication teaches a dosage of 0.1-8,000,000 IU, Applicant makes the following remarks.

Applicant respectfully submits that the '985 publication does not teach the claimed composition or methods of use. In particular, the '985 publication does not teach or suggest a dosage of 2,000,000-4,000,000 JRU (corresponding to 3,000,000-6,000,000 IU) for the treatment of bullous pemphigoid.

The '985 publication describes that ultra-low doses of interferon-γ may be used for the treatment of disease. *See e.g.*, paragraph [0001] ("The present invention relates...to the administration of *ultra-low dosages* of interferon gamma (IFN-γ) to treat a variety of immunopathological states...") (emphasis added). Specifically, the '985 publication discloses the administration of interferon-γ in an amount of 1-8,000 units per kilogram of body weight. *See* abstract and claim 1.

1 IU is equivalent to 1.5 units. *See e.g.*, Physician's Desk Reference at page 1756, under the product ACTIMMUNE®; *see also* July 6, 2003 Response to Office Action for Application No. 09/953,206 at page 5 ("160 IU/kg (240 units/kg)"), attached

[1] This statement appears to conflict with the Office Action's statement that Shachar et al. is silent on the administration of IFN-γ in a daily dose of 200,000-4,000,000 JRU. *See* O.A. at pages 9 and 10. Applicant respectfully requests the USPTO to clarify this issue.

herewith as **Exhibits D and E**, respectively. Thus, for example, 8,000 units per 100 kilograms of body weight would equal 533,333 IU. This dosage amount does not fall between 2,000,000 and 4,000,000 JRU (corresponding to 3,000,000 and 6,000,000 IU). Accordingly, Applicant asserts the '985 publication does not teach the amount of interferon-γ as required by the claims.

**Claim Rejections Under 35 U.S.C. § 103**

Claims 2-4 and 11 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. Pub. No. 20030053985 ("'985 publication").

The Office Action concedes that the '985 publication is silent "regarding the administration via intravenous injection, in a daily dose of 200,000-4,000,000 JRU, or co-administration of an antihistaminic, antiallergic, and/or corticosteroid." *See* O.A. at page 9.

However, the Office Action alleges that one of ordinary skill in the art would know that intravenous injection is a commonly known and practiced method of parenteral administration, and therefore one would have been motivated to administer the interferon-γ compositions of the '985 publication via intravenously. The Office Action also alleges that because antihistaminics, antiallergic, and/or corticosteroid can treat pemphigoid and combining two or more effective agents into one composition is also common and well-known, one of skill in the art would have been motivated to co-administer these compounds with the interferon-γ compositions of the '985 publication. Finally, the Office Action alleges that although the '985 publication does not specifically teach administration of interferon-γ at doses of 200,000-4,000,000, a person of ordinary skill in the art would be motivated and able to optimize the dosage in order to obtain the most favorable clinical outcome. The Office Action opines that such an optimization would be routine for a skilled artisan and is a common component of the treatment of many diseases.

Applicant has cancelled claims 1-8 and 10-11. Applicant submits the above amendments render this rejection moot. To the extent this rejection would apply to claims 9 and 12-17, Applicant makes the following remarks.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See* M.P.E.P. §§ 2142-2143.

Applicant respectfully submits the '985 publication does not teach or suggest the claimed invention. In particular, there is no teaching, suggestion or motivation to modify the '985 publication to arrive at the claimed invention.

The '985 publication describes that ultra-low doses of interferon-γ may be used for the treatment of disease. *See e.g.*, paragraph [0001] ("The present invention relates...to the administration of *ultra-low dosages* of interferon gamma (IFN-γ) to treat a variety of immunopathological states...") (emphasis added). Specifically, the '985 publication discloses the administration of interferon-γ in an amount of 1-8,000 units per kilogram of body weight. *See* abstract and claim 1.

1 IU is equivalent to 1.5 units. *See e.g.*, Physician's Desk Reference at page 1756, under the product ACTIMMUNE®; *see also* July 6, 2003 Response to Office Action for Application No. 09/953,206 at page 5 ("160 IU/kg (240 units/kg)"), attached herewith as **Exhibits D and E**, respectively. Thus, for example, 8,000 units per 100 kilograms of body weight would equal 533,333 IU. This dosage amount does not fall between 2,000,000 and 4,000,000 JRU (3,000,000 and 6,000,000 IU), as required by the claims.

The Office Action fails to provide any teaching or suggestion that would motivate one of ordinary skill in the art to increase the dosage provided by the teaching of the '985 publication to treat bullous pemphigoid. Furthermore, the Office Action does not provide any evidence to suggest that it is routine for a skilled artisan to increase the dosage of interferon-γ for the treatment of any condition, let alone bullous pemphigoid.

The Office Action also fails to provide any teaching or suggestion that would motivate one of ordinary skill in the art to administer interferon-γ in a daily dose intravenously for treating bullous pemphigoid. While it may be true that intravenous injection is a commonly known and practiced method of parenteral administration, the

Office Action does not provide any evidence that one of the skill in the art would have been motivated to administer the interferon-γ compositions of the '985 publication intravenously for treating bullous pemphigoid.

Similarly, the Office Action does not provide the requisite motivation for administering human interferon-γ in combination with an antihistaminic, an antiallergic, a corticosteroid, or any combination thereof. The Office Action does not provide any evidence that one of the skill in the art would have been motivated to administer the interferon-γ compositions of the '985 publication in combination with an antihistaminic, an antiallergic, a corticosteroid, or any combination thereof.

In view of the above, Applicant respectfully asserts the Office Action has not established a *prima facie* case of obviousness and therefore the 35 U.S.C. § 103(a) rejection should be withdrawn.

## CONCLUSION

Applicants respectfully submit that claims 9 and 12-17 are in condition for allowance, and such disposition is earnestly solicited. Should the Examiner believe that any issues remain after consideration of this response, the Examiner is encouraged to contact the Applicant's undersigned representative to discuss and resolve any such issues.

Respectfully submitted,

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